REMARKS/ARGUMENTS

The foregoing amendments in the specification and claims are of a formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-47 were pending in this application and were rejected on various grounds.

With this amendment, Claims 28-31, 34-37 and 39-43 have been canceled without prejudice, Claims 32-33, 38 and 44 have been amended, and new Claim 48 has been added.

Claims 32, 33, 38 and 44-48 are pending after entry of the present amendment. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

The amendments to the specification and claims are fully supported by the specification and claims as originally filed and do not constitute new matter. In addition, new Claim 48 is fully supported by the specification as originally filed. Amendments to Claim 32 can be found in Example 147 of the specification. Support for new Claim 48 can be found at least in Example 150 of the specification.

1. Formal Matters

Applicants thank the examiner for entering the Preliminary Amendments filed on December 12, 2001 and August 29, 2002 into the record.

2. Priority

Applicants thank the Examiner for acknowledging that utility was based upon the detection in the Fetal Hemoglobin Induction in an Erythroblastic Cell Line assay 107 as set forth herein. The Examiner further notes that the disclosure of PRO 1306 utility in this assay is first identified within PCT/US00/04342 filed 2-18-00. Accordingly, the effective filing date for the instant application is that of the PCT/US00/04342 application filed 2-18-2000. Applicants further rely on the chondrocyte re-differentiation assay (Example 150) for patentable utility

which was first disclosed in PCT/US00/04342 filed on February 18, 2000, priority to which has been claimed in this application.

3. Specification

The Examiner notes that the title of the invention is not descriptive. The title of the application has been amended to recite a new, descriptive title indicative of the invention to which the claims are directed.

4. As requested by the Examiner, the specification has been amended to remove embedded hyperlink and/or other forms of browser-executable code.

In addition, Applicants have amended the specification to clearly recite the conditions of the deposits made under the Budapest Treaty.

5. Double Patenting

The Examiner alleges that "there are a series of applications in which SEQ ID NO:109 is present but do not claim the polynucleotide" and that "there is at least one other application filed by the applicants which contains the polynucleotide of SEQ ID NO: 109 which is identical to the polypeptide of SEQ ID NO: 109, and which may contain possible conflicting claims." The Examiner has requested that Applicants point out to the Examiner all double patenting issues.

To the best of our knowledge, Applicants have not filed any applications having claims directed to a polynucleotide of a sequence identical to SEQ ID NO: 109. Applicants believe that the Examiner reached his conclusion of the existence of possible conflicting claims based on the disclosure of the **publications** of other U.S. applications filed by Applicants, which do not reflect the changes made in preliminary amendments in those applications.

6. Deposits of Biological Organisms

Applicants note with appreciation that the Examiner acknowledged the deposit of organisms under accession number ATCC 203231 under the terms of the Budapest Treaty on

International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure in compliance with this requirement.

8. **Claim Rejections Under 35 U.S.C. 112, First Paragraph (Written Description)**

Claims 28-33, 36-37 and 41-47 are rejected under 35 U.S.C. §112, first paragraph, alledgedly for "containing subject matter which was not described in the specification in such a way as to reasonably convey one skilled in the relevant art the inventors, at the time the application was filed, had possession of the invention."

The Examiner notes that the specification describes polynucleotides encoding the peptide sequence consisting of SEQ ID: 195 and 196, which is shown to test positive in the fetal hemoglobin induction in an erythroblastic cell line, however,

> "the claims as written include polynucleotides encoding polypeptides having at least 80-99% sequence identity with SEQ ID NO:110 (sic; SEQ ID NO:196) and polynucleotides encoding polypeptides . . . [with] no particular biological activity, function or hybridization stringency conditions are recited."

Applicants respectfully submit that the cancellation of Claims 28-31, 36-37 and 41-43 renders the rejection of these claims moot.

Without acquiescing to the propriety of this rejection, solely in the interest of expediting prosecution in this case, Applicants respectfully submit that amended Claim 32 (and, as a consequence, those claims dependent from the same) now recite a functional limitation that "the nucleic acid encodes a polypeptide having fetal hemoglobin inducing activity." And, accordingly, it is no longer true that claim 32 is drawn to a genus of polynucleotides defined by sequence identity alone.

Coupled with the general knowledge available in the art at the time of the invention, the specification provides ample written support for such polypeptides in Example 147 (page 522 of the specification) where the assay for the ability of polypeptides to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line are disclosed; and that molecules

testing positive in the assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. Thus, based on the high percentage of sequence identity and the described method to assay for polypeptides that induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line, one skilled in the art would have known at the time of the invention, that the Applicants had possession of the claimed polynucleotides.

The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of the pending claims for allegedly lacking written support.

9. Claim Rejections Under 35 U.S.C. 112, First Paragraph (Enablement)

Claims 28-33, 36-37 and 41-47 are rejected under 35 U.S.C. 112, first paragraph allegedly because "the specification does not reasonably provide enablement for the variable encoding sequences and for such generic sequences where no requisite functional activity is provided as claimed. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." Applicants respectfully disagree and traverse the rejection.

Applicants respectfully submit that the cancellation of claims 28-31, 36-37 and 41-43 renders the rejection of these claims moot.

Without acquiescing to the Examiner's position in the current rejections, and without prejudice to further prosecution of the subject-matter in one or more continuation or divisional applications, Claim 32 (and, as a consequence, those claims dependent from the same) have been amended to recite "wherein the nucleic acid encodes a polypeptide having fetal hemoglobin inducing activity." Since the claimed genus is now characterized by a combination of structural and functional features, any person of skill would know how to make and use the invention without undue experimentation based on the general knowledge in the art at the time the invention was made. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" *In re*

Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

10. Claim Rejection Under 35 U.S.C. 112, Second Paragraph

Claims 28-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the Examiner objects to the Applicants' use of the terms "extracellular domain" and "lacking its associated signal peptide." The Examiner further asserts that the use of the term "stringent conditions" is indefinite.

Applicants submit that the cancellation of Claims 28-31, 34-37 and 39-43 renders the rejection of these claims moot.

Without acquiescing to the Examiner's position, and solely in the interest of expediting prosecution in this case, as amended, the terms "extracellular domain" and "extracellular domain ... lacking its associated signal peptide" are no longer present in Claims 32-33 (and, as a consequence, those claims dependent from the same). Hence, the rejection is believed to be moot, and should be withdrawn.

11. Claim Rejection Under 35 U.S.C. 102

Claims 28-31 and 41-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Hillman et al., U.S. 6,135,941, October 24, 2000 (with an effective priority date of March 27, 1998).

Applicants submit that the cancellation of Claims 28-31 and 41-43 renders the rejection of these claims moot.

Further, Claim 44 (and, as a consequence, those claims dependent from the same) has been amended to be dependent on Claim 32. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 44-47 under 35 U.S.C. §102(e).

CONCLUSION

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-2830 P1C52**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: January 11, 2005 By: _____
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